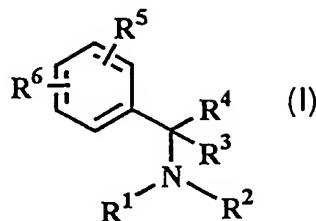


CLAIMS

1. A compounds of formula (I)



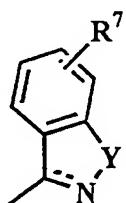
wherein R¹ and R², which may be the same or different, are each selected from C₆₋₁₂aryl, C₂₋₁₄heteroaryl, C₆₋₁₂arylC₁₋₆alkyl, C₂₋₁₄heteroarylC₁₋₆alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from C₁₋₆alkoxy, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₄₋₆cycloalkenyl, C₆₋₁₂aryl, C₂₋₁₄heteroaryl, halogen, amino, hydroxy, haloC₁₋₆alkyl, nitro, C₁₋₆alkylthio, sulphonamide, C₁₋₆alkylsulphonyl, hydroxy-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl, carboxyl, carboxyC₁₋₆alkyl, carboxamide and C₁₋₆alkylcarboxamide), hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₄₋₆cycloalkenyl, C₂₋₆alkenyl, C₂₋₆alkynyl and C₁₋₆alkoxyC₁₋₆alkyl (where the alkyl, cycloalkyl, cycloalkenyl, alkenyl, alkynyl, or alkoxyalkyl moieties may be optionally substituted by one or more substituents selected from amino, halogen, hydroxy, C₁₋₆alkylcarboxamide, carboxamide, carboxy, C₁₋₆alkoxycarbonyl, C₁₋₆alkylcarboxy and carboxyC₁₋₆alkyl) or one of R¹ and R² are as hereinbefore defined and one is hydroxy;

R³ and R⁴, which may be the same or different, are each selected from C₆₋₁₂aryl, C₂₋₁₄heteroaryl, C₆₋₁₂arylC₁₋₆alkyl, C₂₋₁₄heteroarylC₁₋₆alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from C₁₋₆alkoxy, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₄₋₆cycloalkenyl, C₆₋₁₂aryl, C₂₋₁₄heteroaryl, halogen, amino, hydroxy, haloC₁₋₆alkyl, nitro, C₁₋₆alkylthio, sulphonamide, C₁₋₆alkylsulphonyl, hydroxy-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl, carboxyl, carboxyC₁₋₆alkyl, C₁₋₆alkylcarboxamide and carboxamide), hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkylC₁₋₆alkyl, C₄₋₆cycloalkenyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy-C₁₋₆alkyl, haloC₁₋₆alkyl, haloC₂₋₆alkenyl, haloC₂₋₆alkynyl, cyano, carboxyl, C₁₋₆alkylcarboxy and carboxyC₁₋₆alkyl (where the alkyl, cycloalkyl, cycloalkenyl, alkenyl, alkynyl, or alkoxyalkyl moieties may be optionally

substituted by one or more substituents selected from amino, hydroxy, C₁₋₆alkylcarboxamide, carboxamide, carboxy, C₁₋₆alkoxycarbonyl, C₁₋₆alkylcarboxy and carboxyC₁₋₆alkyl); or one of R³ or R⁴ together with one of R¹ or R² and the N atom to which it is attached form a 5- or 6-membered heterocyclic ring.

R⁵ represents one or more ring substituents selected from halogen, hydrogen C₁₋₆alkyl and C₁₋₆alkoxy; and

R⁶ represents a single ring substituent of formula:



wherein the dotted line represents an optional bond; Y is oxygen or -NR⁸

(where R⁸ is hydrogen or C₁₋₆alkyl) and R⁷ represents one or more substituents selected from hydrogen, halogen, haloC₁₋₆alkyl, C₁₋₆alkyl and C₁₋₆alkoxy; or
a pharmaceutically acceptable salt or solvate thereof.

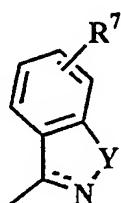
2. A compound according to claim 1 wherein R¹ and R², which may be the same or different, are each independently selected from C₆₋₁₂aryl, C₂₋₁₄heteroaryl, C₆₋₁₂arylC₁₋₆alkyl, C₂₋₁₄heteroarylC₁₋₆alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from C₁₋₆alkoxy, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₄₋₆cycloalkenyl, C₆₋₁₂aryl, C₂₋₁₄heteroaryl, halogen, amino, hydroxy, haloC₁₋₆alkyl, nitro, C₁₋₆alkylthio, sulphonamide, C₁₋₆alkylsulphonyl, hydroxyC₁₋₆alkyl, carboxyl, carboxy-C₁₋₆alkyl, carboxamide and C₁₋₆alkylcarboxamide), hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₄₋₆cycloalkenyl, C₂₋₆alkenyl, C₂₋₆alkynyl and C₆₋₁₂alkoxyC₁₋₆alkyl (where the alkyl, cycloalkyl, cycloalkenyl, alkynyl, or alkoxyalkyl moieties may be optionally substituted by one or more substituents selected from amino, hydroxy, C₁₋₆alkylcarboxamide, carboxamide, carboxy and carboxyC₁₋₆alkyl) or one of R¹ and R² are as hereinbefore defined and one is hydroxy;

R³ and R⁴, which may be the same or different, are each independently selected from C₆₋₁₂aryl, C₂₋₁₄heteroaryl, C₆₋₁₂arylC₁₋₆alkyl,

C_{2-14} heteroaryl- C_{1-6} alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from C_{1-6} alkoxy, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{4-6} cycloalkenyl, C_{6-12} aryl, C_{2-14} heteroaryl, halogen, amino, hydroxy, halo C_{1-6} alkyl, nitro, C_{1-6} alkylthio, sulphonamide, C_{1-6} alkylsulphonyl, carboxamide and C_{1-6} alkylcarboxamide), hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{4-6} cycloalkenyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy C_{1-6} alkyl, cyano, carboxyl and carboxy C_{1-6} alkyl;

R^5 represents one or more ring substituents selected from halogen, hydrogen, C_{1-6} alkyl and C_{1-6} alkoxy; and

R^6 represents a single ring substituent of formula:



wherein the dotted line represents an optional bond; Y is oxygen or -NR⁸ (where R⁸ is hydrogen or C₁₋₆alkyl) and R⁷ is hydrogen, halogen, C₁₋₆alkyl or C₁₋₆alkoxy;or a pharmaceutically acceptable salt or solvate thereof.

3. A compound according to claim 1 or 2 wherein one of R¹ and R² is hydrogen and the other is C₆₋₁₂arylC₁₋₆alkyl (where the alkyl or aryl moiety may be optionally substituted by one or more ring substituents selected from C₁₋₆alkoxy and C₂₋₁₄heteroaryl); R³,R⁴ and R⁵ are hydrogen, Y is oxygen, the dotted line represents a bond and R⁷ is hydrogen or halogen; or a pharmaceutically acceptable salt or solvate thereof.
4. A compound of formula (I) according to any of claims 1 to 3 wherein R¹ and R² are both hydrogen; one of R³ and R⁴ is hydrogen and the other is C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxyC₁₋₆alkyl or C₆₋₁₂arylalkyl; R⁵ is hydrogen, Y is oxygen or -NCH₃, the dotted line represents a bond and R⁷ is hydrogen or halogen; or a pharmaceutically acceptable salt or solvate thereof.

- 5 A compound according to claim 1 selected from:
2-(1,2-Benzisoxazol-3-yl)-benzenemethanamine;
2-(1,2-Benzisoxazol-3-yl)- α -2-propenyl-benzenemethanamine;
(R)-(+)-2-(1,2-Benzisoxazol-3-yl)- α -2-propenyl-benzenemethanamine;
(S)-(-)-2-(1,2-Benzisoxazol-3-yl)- α -2-propenyl-benzenemethanamine;
2-(1,2-Benzisoxazol-3-yl)- α -butyl-benzenemethanamine;
2-(1,2-Benzisoxazol-3-yl)- α -2-propynyl-benzenemethanamine;
2-(1-Methyl-1*H*-indazol-3-yl)- α -2-propenyl-benzenemethanamine;
(-)-2-(6-chloro-1,2-benzisoxazol-3-yl)- α -2-propynyl-
benzenemethanamine;
(S)-(-)-2-(6-chloro-1,2-benzisoxazol-3-yl)- α -2-propenyl-benzene-
methanamine;
and pharmaceutically acceptable salts and solvates thereof.
6. A compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to any of claims 1 to 54 for use in therapy.
7. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to any of claims 1 to 5, in the manufacture of a medicament for the treatment or prevention of depression.
8. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to any of claims 1 to 5, in the manufacture of a medicament for the treatment or prevention of conditions selected from:
 - anxiety disorders, including phobic neuroses, panic neuroses, anxiety neuroses, post-traumatic stress disorder and acute stress disorder;
 - attention deficit disorders;
 - eating disorders, including obesity, anorexia nervosa and bulimia;
 - personality disorders, including borderline personality disorders;
 - schizophrenia and other psychotic disorders, including schizo affective disorders, dilusional disorders, shared psychotic disorder, brief psychotic disorder and psychotic disorder;
 - narcolepsy-cataplexy syndrome;
 - substance related disorders;
 - sexual function disorders; and
 - sleep disorders.

9. A pharmaceutical formulation comprising a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to claim 1, together with a pharmaceutically acceptable carrier thereof.

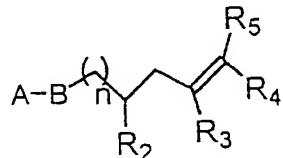
10. A method for the treatment or prevention of a psychiatric disorder in an animal, which comprises administering to said animal an effective amount of an I_h channel modulator.

11. A method according to claim 10, wherein the psychiatric disorder is depression, anxiety or psychosis.

12. A method according to claim 10, wherein the I_h channel modulator blocks conductance of the I_h channel and/or the open probability.

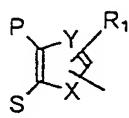
13. A method according to claim 12, wherein the I_h channel modulator has a pIC_{50} of 5 to 12 in an I_h channel modulator functional assay.

14. A compound of formula (I)

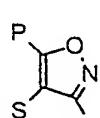


(I)

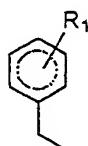
wherein A is a group selected from (a), (b) or (c):



or



or



(a)

(b)

(c)

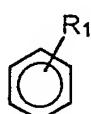
wherein Y is CH or N;

X is O, S, CH=CH, or CH=N;

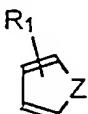
P and S, which may be the same or different, each represent hydrogen, C₁₋₄alkyl, C₁₋₃alkoxy, cyano, halogen, trifluoromethyl, phenyl or pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C₁₋₃alkyl; or P and S together with the ethylene group to which they are bonded form a 1,2-phenylene, a pyridinediyl (including 2,3- and 3,4-pyridinediyl), or a 1-cyclohexen-1,2-diyl group, which groups may be optionally substituted by one or more substituents selected from hydrogen, C₁₋₄alkyl, C₁₋₃alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C₁₋₃alkyl;

R₁ represents one or more ring substituents selected from hydrogen, C₁₋₄alkyl, C₁₋₃alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C₁₋₃alkyl;

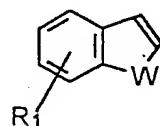
B is a bivalent radical derived from an aromatic group selected from (d), (e) or (f):



(d)



(e)



(f)

wherein

Z is O or S;

W is O, S or CH=CH,

R₁ is as hereinbefore defined;

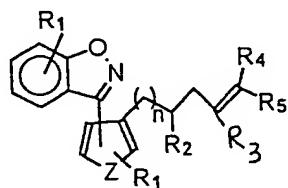
R₂ is NH₂;

R₃, R₄, and R₅, which may be the same or different, each represent halogen, C₁₋₄alkyl or hydrogen, or R₄ and R₅ together form a carbon-carbon bond;

n is 0 or 1;

or a physiologically acceptable salt or solvate thereof; with the proviso that when A is group (b) wherein P and S together with the ethylene group to which they are bonded form a 1,2-phenylene group, which group may optionally be substituted by one or more substituents selected from hydrogen, C₁₋₄alkyl, C₁₋₃alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C₁₋₃alkyl; R₂, R₃, R₄ and R₅ are as herein before defined and n is 0; then B is a group (e) or (f).

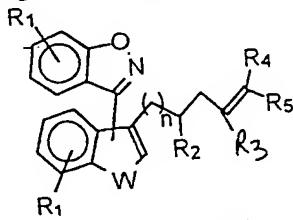
15. A compound according to claim 14 of formula (IA)



(IA)

wherein Z, R₁, R₂, R₃, R₄ and R₅ are as defined in claim 14 and n is 0;
or a physiologically acceptable salt or solvate thereof.

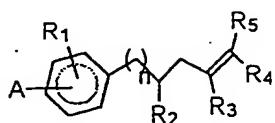
16. A compound according to claim 14 of formula (IB)



(IB)

wherein W, R₁, R₂, R₃, R₄ and R₅ are as defined in claim 14 and n is 0;
or a physiologically acceptable salt or solvate thereof.

17. A compound according to claim 14 of formula (IC)



(IC)

wherein A, R₁, R₂, R₃, R₄ and R₅ are as defined in claim 1 and n is 0 or 1, preferably n is 0; or a physiologically acceptable salt of solvate thereof; with the proviso that A is not a group (b) wherein P and S together with the ethylene group to which they are bonded form a 1,2-phenylene group, which group may be optionally substituted by one or more substituents selected from hydrogen, C₁₋₄alkyl, C₁₋₃alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C₁₋₃alkyl; R₂, R₃, R₄ and R₅ are as defined in claim 1 and n is 0;

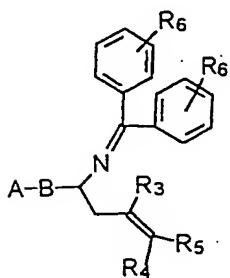
or a physiologically acceptable salt or solvate thereof.

18. A pharmaceutical formulation containing a compound of formula (I) or a physiologically acceptable salt or solvate thereof, as defined according to claim 14, together with a pharmaceutically acceptable carrier therefor.

19. A method for the treatment or prevention of a psychiatric disorder in an animal, which comprises administering to said animal an effective amount of a compound of formula (I) or a physiologically acceptable salt or solvate thereof, as defined according to claim 14.

20. A process for preparing a compound of formula (I) as defined in claim 14 or a physiologically acceptable salt or solvate thereof; which comprises:

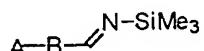
(A) reacting a compound of formula (II)



(II)

wherein A, B, R₃, R₄ and R₅ are as defined in claim 1 and R₆ is hydrogen or halogen, with a hydrolysing agent;

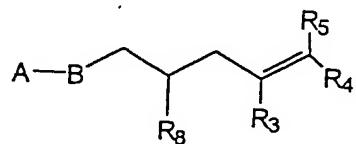
(B) reacting an imine of formula (IIIA)



(IIIA)

wherein A and B are as defined in claim 10, with an appropriate organometallic reagent in the presence of an inert solvent; or

(C) for compounds of formula (I) wherein n is 1, the reduction of a compound of formula (XV)



(XV)

wherein A, B, R₃, R₄ and R₅ are as defined in claim 1 and R₈ is an azido group, and

where necessary or desired, following processes A to C above, any one or more of the following further steps in any order may be performed:

- (i) removing any remaining protecting group(s);
- (ii) converting a compound of formula (I) or a protected form thereof into a further compound of formula (I) or a protected form thereof;
- (iii) converting a compound of formula (I) or a protected form thereof into a pharmaceutically acceptable salt or solvate of a compound of formula (I) or a protected form thereof;
- (iv) converting a pharmaceutically acceptable salt or solvate of a compound of formula (I) or a protected form thereof into a compound of formula (I) or a protected form thereof;
- (v) converting a pharmaceutically acceptable salt or solvate of a compound of formula (I) or a protected form thereof into another pharmaceutically acceptable salt or solvate of formula (I);
- (vi) where the compound of formula (I) is obtained as a mixture of (R) and (S) enantiomers resolving the mixture to obtain the desired enantiomer;
- (vii) cleavage of a compound of formula (I) from a solid phase resin.

21. A method for identifying compounds useful for the treatment or prevention of psychiatric disorders by measuring the level of I_h channel modulation in an I_h channel modulation assay.

22. A method for identifying compounds useful for the treatment or prevention of psychiatric disorders by measuring the level of I_h channel modulation in an I_h channel modulation assay comprising:

- taking a brain slice, or a cultured brain slice, or ganglia of the peripheral nervous system, or primary

- cell cultures of central and/or peripheral nervous tissue, or cell lines expressing I_h channels
- incubating and/or exposing these cells and tissues to test compounds and
- measuring whether these test compounds affect conductance of the I_h channel and/or the open probability.